

for an isolated polynucleotide that is at least 90% homologous to the nucleotide sequence of SEQ ID NO. 1 or an isolated polynucleotide capable of hybridizing under the conditions set forth in claim 1 to the sequence of SEQ ID NO. 1. The Examiner urges that because the Bowie et al. reference shows that predicting protein structure from sequence data and using it to predict structural determination to ascertain functional aspects of the protein is complex, and because the Mikayama et al. and Voet et al. references demonstrate that the change of a single amino acid has the potential to alter protein function, there is a high degree of unpredictability in the protein art. He then concludes that the Specification does not provide sufficient guidance to make or use the variant or mutated polypeptide species encoded by the claimed polynucleotides.

The Examiner has rejected Applicants' argument that the Specification provides enablement by describing functional assays for the sequence variants encompassed by the claim. The Examiner indicates that the addition of a functional limitation requiring that the polynucleotide encodes an amino acid sequence which is an outwardly rectifying potassium channel would obviate this rejection.

Applicants have amended the claims to include the limitation suggested by the Examiner. Thus, Applicants respectfully request reconsideration and removal of the rejection.

#### *Written Description*

The Examiner rejects claims 1-6, 18-30 and 59-61 as containing subject matter which was not described in the Specification in such a way to reasonably convey to the skilled artisan that Applicants had possession of the claim invention at the time the Application was filed. The Examiner notes that the present claims contain are genus claims and that the Specification discloses that the mutated polynucleotide may be a polynucleotide having a nucleotide sequence encoding a potassium channel with an amino acid sequence that has been changed at one or more positions. He further notes that the Specification and claims do not indicate the distinguishing attribute shared by the members of the genus and that the genus is highly variable because a significant number of structural differences between genus members are permitted.

The Examiner has rejected Applicants' argument that the functional assays for the sequence variants described by the Specification provides sufficient written description. The Examiner contends that the functional limitation requiring the polynucleotide to encode an amino acid sequence having activity as

a KCNQ4 potassium channel subunit is insufficient to describe the claimed genus since it is unclear which activity of a KCNQ4 potassium channel is required. The Examiner indicates, however, that the addition of a functional limitation to the claim that requires the polynucleotide to encode an amino acid sequence which is an outwardly rectifying potassium channel would obviate this rejection.

Applicants have introduced an amendment into the claims that limits the encoded amino acid sequence to an outwardly rectifying potassium channel. Applicants thereby request reconsideration and removal of the rejection.

Rejections Under 35 U.S.C § 112, second paragraph

The Examiner has rejected claims 10 and 21 for lack of sufficient antecedent basis for the limitation "said variant," which appears in line 2 of the claims.

Applicants have amended claims 10 and 21 to provide appropriate antecedent basis. Specifically, Applicants have deleted the phrase "said variant" and replaced it with the appropriate term "polynucleotide." Applicants therefore request reconsideration and removal of the rejection.

In view of the above remarks, all of the claims remaining in the case are submitted as defining non-obvious, patentable subject matter.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a one (1) month extension of time for filing a response in connection with the present application and the required fee of \$110.00 is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Gerald M. Murphy, Jr. (Reg. No. #28,977) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

**Attached hereto is a marked-up version of the changes made to the application by this Amendment.**

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By *[Signature]* # 47,604  
for Gerald M. Murphy, Jr. (#28,977)

GMM/SWG/sbp  
2815-0127P

P.O. Box 747  
Falls Church, VA 22040-0747  
(703) 205-8000

Attachment: Version with Markings to Show Changes Made

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner of Patents and Trademarks, Washington

D.C. 20261 on: 02-21-03  
(Date of deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

*[Signature]*  
(Signature)  
02-21-03  
(Date of Signature)

VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE CLAIMS:

The claims have been amended as follows:

1. (Four Amended) An isolated polynucleotide having a nucleic acid sequence which is capable of hybridizing under high stringency conditions with the polynucleotide sequence of SEQ ID NO: 1, or its complementary strand, wherein said hybridizing occurs in a solution of 5 X SSC, 5 X Denhardt's solution, 0.5% SDS and 100 µg/ml of denatured sonicated salmon sperm DNA for 12 hours at approximately 45°C followed by washing twice for 30 minutes in 2 X SSC, 0.5% SDS at a temperature of at least 65°C, wherein said polynucleotide encodes an amino acid sequence ~~having activity as~~ which is a sub-unit of a KCNQ4 potassium channel subunit which is an outwardly rectifying potassium channel.
10. (Thrice Amended) The isolated polynucleotide according to claim 7, wherein said ~~variant~~ polynucleotide ~~has~~ encodes an amino acid sequence that has been changed at one or more positions located in a conserved region, wherein said region is defined by Table 1.
21. (Thrice Amended) The cell according to claim 18, wherein said ~~variant~~ heterologous polynucleotide ~~has~~ encodes an amino acid sequence that has been changed at one or more positions located in a conserved region, wherein said region is defined by Table 1.